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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/699,097

**Applicant(s)**

HUANG ET AL.

**Examiner**

DUSTIN Q. DAM

**Art Unit**

1795

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-26 and 43-46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-26 and 43-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S508)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 6, 2009 has been entered.
2. In view of the Amendments to the Claims filed February 6, 2009, the rejections of claims 1-26 under 35 U.S.C. 102(b) and 103(a) previously presented in the Office Action sent October 28, 2008 have been withdrawn.
3. Claims 1-26 and 43-46 are currently pending and have been fully considered.

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 15-17 and 19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by WIKTOROWICZ et al. (U.S. Patent 6,214,191 B1).
  - a. With regards to claim 15, WIKTOROWICZ et al. discloses an integrated microfluidic device comprising a sample unloading chamber (160, FIG. 3) and a fluid

reservoir (130, FIG. 4) connected by a microfluidic channel (180, FIG. 3), wherein the microfluidic channel comprises an inlet and an outlet (FIG. 3 shows inlet of channel 180 at end towards 130 and outlet at end towards 160), the sample unloading chamber is configured to be structurally capable of unloading a sample of charged molecules from the microfluidic device (160, FIG. 4 & see line 61-64, column 6 "liquid loading region 160 at upper end of the plate, for conveniently introducing and removing separation media to and from the separation cavity"), is positioned at the outlet of the microfluidic channel (FIG. 3), and comprises a first electrode (135, FIG. 3 is port for electrode, see line 57-58, column 15) and a second electrode (132, FIG. 3 is port for electrode, see line 44-47, column 7 "132a" or wire electrode spanning across and into separation cavity via port 132, see line 52-56, column 15) configured to be structurally capable of generating a first electric field in the sample unloading chamber, the sample unloading chamber defining an opening in the microfluidic device (opening formed by plate 122 & 120 at region 160, FIG. 4) wherein at least a portion of the first and second electrodes is in the opening (see line 49-58, column 15 which discloses point or wire electrodes at 132 and 135) and wherein, when generated, the first electric field is configured to transfer charged molecules from the outlet of the microfluidic channel into the sample unloading chamber, and the fluid reservoir is positioned at the inlet of the microfluidic channel (FIG. 3) and comprises a third electrode (130, FIG. 3 is port for electrode, see line 38-44, column 7 "130a") configured to be structurally capable of generating a second electric field with at least the second electrode.

- b. With regards to claim 16, WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are nucleic acid molecules (line 9, column 2).
- c. With regards to claim 17, WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the nucleic acid molecules are deoxyribonucleic acids (line 17-26, column 12 "blood" inherently comprises DNA).
- d. With regards to claim 19, WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are proteins (line 10, column 2).

*Claim Rejections - 35 USC § 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- 1. Determining the scope and contents of the prior art.
  - 2. Ascertaining the differences between the prior art and the claims at issue.
  - 3. Resolving the level of ordinary skill in the pertinent art.
  - 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
8. Claims 20-22, 24, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIKTOROWICZ et al. (U.S. Patent 6,214,191 B1).

a. With regards to claims 20 and 46, WIKTOROWICZ et al. discloses an integrated microfluidic device comprising a sample unloading chamber (160, FIG. 3) and a fluid reservoir (130, FIG. 4) connected by a microfluidic channel (180, FIG. 3), wherein the microfluidic channel comprises an inlet and an outlet (FIG. 3 shows inlet of channel 180 at end towards 130 and outlet at end towards 160), the sample unloading chamber is configured to be structurally capable of unloading a sample of charged molecules from the microfluidic device (160, FIG. 4 & see line 61-64, column 6 "liquid loading region 160 at upper end of the plate, for conveniently introducing and removing separation media to and from the separation cavity"), is positioned at the outlet of the microfluidic channel (FIG. 3), and comprises a first electrode (135, FIG. 3 is port for electrode, see line 57-58, column 15) and a second electrode (132, FIG. 3 is port for electrode, see line 44-47, column 7 "132a" or wire electrode spanning across and into separation cavity via port 132, see line 52-56, column 15) configured to be structurally capable of generating a first electric field in the sample unloading chamber, and a section of separation media in the sample unloading chamber (line 11-15, column 16), the sample unloading chamber defining an opening in the microfluidic device (opening formed by plate 122 & 120 at region 160, FIG. 4) wherein at least a portion of the first and second electrodes is in the opening (see line 49-58, column 15 which discloses point or wire electrodes at 132 and 135) and wherein, when generated, the first electric field is configured to transfer charged molecules from the outlet of the microfluidic channel into the sample unloading chamber, and the fluid reservoir is positioned at the inlet of the microfluidic channel (FIG. 3) and comprises a third electrode (130, FIG. 3 is port for electrode, see line 38-44, column 7

"130a") configured to be structurally capable of generating a second electric field with at least the second electrode.

WIKTOROWICZ et al. also does not appear to explicitly comprise a single embodiment correlated with the referenced Figures which discloses the use of a matrix material in the sample unloading chamber.

However, WIKTOROWICZ et al. discloses the use of two different separation media in each separation zone, the cited sample unloading zone 160 being the first of the two zones (line 11-15, column 16). WIKTOROWICZ et al. also discloses it is "conventional" to use a matrix material as a separation media particularly in the first separation zone (line 24-27, column 2).

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the specific embodiments of WIKTOROWICZ et al. referenced to the Figures and include a matrix material in the sample unloading chamber because WIKTOROWICZ et al. suggests different materials may be used in two dimensional electrophoreses in which conventionally matrix materials are used as separation media which would provide for expected predictable results in the combination and because matrix materials are well known in the art specifically as separation media in which the simple substitution of a known element known in the art for the performing the same function is matter of obviousness; e.g. separation media substitution (See MPEP 2141 {III} {B}). Modified WIKTOROWICZ et al. provides for the matrix material to only be present in the sample loading chamber, especially since

WIKTOROWICZ et al. discloses the use to different separation media in each separation zone.

b. With regards to claim 21, independent claim 20 is obvious over WIKTOROWICZ et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are nucleic acid molecules (line 9, column 2).

c. With regards to claim 22, independent claim 20 and dependent claim 21 are obvious over WIKTOROWICZ et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the nucleic acid molecules are deoxyribonucleic acids (line 17-26, column 12 "blood" inherently comprises DNA).

d. With regards to claim 24, independent claim 20 is obvious over WIKTOROWICZ et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are proteins (line 10, column 2).

e.

9. Claims 1-7, 9, 10, 13, and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIKTOROWICZ et al. (U.S. Patent 6,214,191 B1) in view of NORDMAN et al. (U.S. PG-Pub 2002/0162745 A1).

a. With regards to claims 1 and 43, WIKTOROWICZ et al. discloses an integrated microfluidic device comprising a sample loading chamber (160, FIG. 3) and a fluid reservoir (140, FIG. 4) connected by a microfluidic channel (170, FIG. 3), wherein the



microfluidic channel comprises an inlet and an outlet (FIG. 3 shows inlet of channel 170 at end towards 160 and outlet at end towards 140), the sample loading chamber is configured to be structurally capable of loading a sample of charged molecules into the microfluidic device (160, FIG. 4 & see line 61-64, column 6 "liquid loading region 160 at upper end of the plate, for conveniently introducing and removing separation media to and from the separation cavity"), is positioned at the inlet of the microfluidic channel (FIG. 3) and comprises a first electrode (135, FIG. 3 is port for electrode, see line 57-58, column 15) and a second electrode (132, FIG. 3 is port for electrode, see line 44-47, column 7 "132a" or wire electrode spanning across and into separation cavity via port 132, see line 52-56, column 15) configured to be structurally capable of generating a first electric field in the sample loading chamber, the sample loading chamber defining an opening in the microfluidic device (opening formed by plate 122 & 120 at region 160, FIG. 4) wherein at least a portion of the first and second electrodes is in the opening (see line 49-58, column 15 which discloses point or wire electrodes at 132 and 135) and wherein, when generated, the first electric field is configured to transfer charged molecules in the sample loading chamber to the inlet of the microfluidic channel, and the fluid reservoir is configured to be structurally capable of unloading a sample of charged molecules from the microfluidic device (via slot 140, FIG. 4), is positioned at the outlet of the microfluidic channel (FIG. 3) and comprises a third electrode (140, FIG. 4 is port for electrode, see line 57-58, column 15) configured to be structurally capable of generating a second electric field with at least the second electrode. WIKTOROWICZ et al. also discloses it may be desirable for sample detection after electrophoresis in the

second dimension (line 32-38, column 4) which may include optical detection (line 43-56, column 16).

WIKTOROWICZ et al. does not appear to explicitly disclose an integrated microfluidic device wherein the fluid reservoir is configured to unload a sample of “separated” charged molecules.

However, NORDMAN et al. discloses a channel electrophoresis device and discloses modifying the interface between the microchannels (14, FIG. 1 & 2) and the fluid reservoir (30, FIG. 1 & 2) such as depicted in FIG. 1 and FIG. 2 in order to control distortion of separated sample to enhance detectability (ABSTRACT).

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the interface between the microchannel outlets and fluid reservoir of WIKTOROWICZ et al. in the same manner as NORDMAN et al. because it would control separated sample distortion which leads to enhanced detection. The combination of WIKTOROWICZ et al. and NORDMAN et al. provides a fluid reservoir configured for unloading separated charged molecules since the separated sample exiting the microchannels of WIKTOROWICZ et al. into the fluid reservoir, as modified by NORDMAN et al., would remain separated.

b. With regards to claim 2, independent claim 1 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are nuclei acid molecules (line 9, column 2).

- c. With regards to claim 3, independent claim 1 and dependent claim 2 are obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the nucleic acid molecules are deoxyribonucleic acids (line 17-26, column 12 "blood" inherently comprises DNA).
- d. With regards to claim 4, independent claim 1 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are proteins (line 10, column 2).
- e. With regards to claims 5, 44, and 45, WIKTOROWICZ et al. discloses an integrated microfluidic devices comprising a sample loading chamber (160, FIG. 3) and a fluid reservoir (140, FIG. 4) connected by a microfluidic channel (170, FIG. 3), wherein the microfluidic channel comprises an inlet and an outlet (FIG. 3 shows inlet of channel 170 at end towards 160 and outlet at end towards 140), the sample loading chamber is configured to be structurally capable of loading a sample of charged molecules into the microfluidic device (160, FIG. 4 & see line 61-64, column 6 "liquid loading region 160 at upper end of the plate, for conveniently introducing and removing separation media to and from the separation cavity"), is positioned at the inlet of the microfluidic channel (FIG. 3) and comprises a first electrode (135, FIG. 3 is port for electrode, see line 57-58, column 15) and a second electrode (132, FIG. 3 is port for electrode, see line 44-47, column 7 "132a" or wire electrode spanning across and into separation cavity via port 132, see line 52-56, column 15) configured to be structurally capable of generating a first

electric field in the sample loading chamber, and a separation media located in the sample loading chamber (line 11-15, column 16) wherein, the sample loading chamber defining an opening in the microfluidic device (opening formed by plate 122 & 120 at region 160, FIG. 4) wherein at least a portion of the first and second electrodes is in the opening (see line 49-58, column 15 which discloses point or wire electrodes at 132 and 135) and when generated, the first electric field is configured to transport the charged molecules from the separation media and to transfer the charged molecules to the inlet of the microfluidic channel, and the fluid reservoir is configured to be structurally capable of unloading a sample of charged molecules from the microfluidic device (via port 140, FIG. 40), is positioned at the outlet of the microfluidic channel (FIG. 3) and comprises a third electrode (140, FIG. 4 is port for electrode, see line 57-58, column 15) configured to be structurally capable of generating a second electric field with at least the second electrode. WIKTOROWICZ et al. also discloses it may be desirable for sample detection after electrophoresis in the second dimension (line 32-38, column 4) which may include optical detection (line 43-56, column 16).

WIKTOROWICZ et al. does not appear to explicitly disclose an integrated microfluidic device wherein the fluid reservoir is configured to unload a sample of “separated” charged molecules. WIKTOROWICZ et al. also does not appear to explicitly comprise a single embodiment correlated with the referenced Figures which discloses the use of a matrix material in the sample loading chamber.

However, WIKTOROWICZ et al. discloses the use of two different separation media in each separation zone, the cited sample loading zone 160 being the first of the

two zones (line 11-15, column 16). WIKTOROWICZ et al. also discloses it is "conventional" to use a matrix material as a separation media particularly in the first separation zone (line 24-27, column 2). NORDMAN et al. discloses a channel electrophoresis device and discloses modifying the interface between the microchannels (14, FIG. 1 & 2) and the fluid reservoir (30, FIG. 1 & 2) such as depicted in FIG. 1 and FIG. 2 in order to control distortion of separated sample to enhance detectability (ABSTRACT).

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the interface between the microchannel outlets and fluid reservoir of WIKTOROWICZ et al. in the same manner as NORDMAN et al. because it would control separated sample distortion which leads to enhanced detection. The combination of WIKTOROWICZ et al. and NORDMAN et al. provides a fluid reservoir configured for unloading separated charged molecules since the separated sample exiting the microchannels of WIKTOROWICZ et al. into the fluid reservoir, as modified by NORDMAN et al., would remain separated. At the time of the invention, it would have also been obvious to a person having ordinary skill in the art to modify the specific embodiments of WIKTOROWICZ et al. referenced to the Figures and include a matrix material in the sample loading chamber because WIKTOROWICZ et al. suggests different materials may be used in two dimensional electrophoreses in which conventionally matrix materials are used as separation media which would provide for expected predictable results in the combination and because matrix materials are well known in the art specifically as separation media in which the simple substitution of a

known element known in the art for the performing the same function is matter of obviousness; e.g. separation media substitution (See MPEP 2141 {III} {B}). The combination of WIKTOROWICZ et al. and NORDMAN et al. provides for the matrix material to only be present in the sample loading chamber, especially since WIKTOROWICZ et al. discloses the use to different separation media in each separation zone.

f. With regards to claim 6, independent claim 5 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above.

WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are nucleic acid molecules (line 9, column 2).

g. With regards to claim 7, independent claim 5 and dependent claim 6 are obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the nucleic acid molecules are deoxyribonucleic acids (line 17-26, column 12 “blood” inherently comprises DNA).

h. With regards to claim 9, independent claim 5 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged molecules are proteins (line 10, column 2).

i. With regards to claim 10, independent claim 5 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the charged

molecules are polypeptide (line 8-12, column 2) sodium dodecyl sulfate supra molecules (line 29-34, column 2 "SDS").

- j. With regards to claim 13, independent claim 5 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device wherein the sample chamber comprises three electrodes (line 52-58, column 15).
10. Claims 18 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIKTOROWICZ et al. (U.S. Patent 6,214,191 B1) in view of ADCOCK (U.S. Patent 4,959,133).

a. With regards to claim 18, independent claim 15 and dependent claim 17 are clearly anticipated by WIKTOROWICZ et al. under 35 U.S.C. 102(b) as discussed above. WIKTOROWICZ et al. discloses an integrated microfluidic device comprising a plurality of electrodes.

WIKTOROWICZ et al. does not appear to explicitly disclose an integrated microfluidic device wherein the DNA is greater than about 50 kilobases in size.

However, ADCOCK discloses a method of filed inversion electric pulses to force DNA or protein out of a gel and into an appropriate receiver (ABSTRACT). The inverted pulsed electric field allows for the electro-elution of higher molecular weights (line 57-60, column 2 such as "larger in molecular weight than  $2 \times 10^4$  base pairs").

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the integrated microfluidic device, as disclosed by WIKTOROWICZ et al., to include applying an inverted pulsed electric field, as disclosed

by ADCOCK, because the inverted pulsed electric field allows for the electro-elution of higher molecular weights.

b. With regards to claim 23, independent claim 20 and dependent claim 22 are obvious over WIKTOROWICZ et al. under 35 U.S.C. 103(a), as applied to claims 20-22, 24, and 46, as discussed above. Modified WIKTOROWICZ et al. discloses an integrated microfluidic device comprising a plurality of electrodes.

WIKTOROWICZ et al. does not appear to explicitly disclose an integrated microfluidic device wherein the DNA is greater than about 50 kilobases in size.

However, ADCOCK discloses a method of filed inversion electric pulses to force DNA or protein out of a gel and into an appropriate receiver (ABSTRACT). The inverted pulsed electric field allows for the electro-elution of higher molecular weights (line 57-60, column 2 such as "larger in molecular weight than  $2 \times 10^4$  base pairs").

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the integrated microfluidic device, as disclosed by modified WIKTOROWICZ et al., to include applying an inverted pulsed electric field, as disclosed by ADCOCK, because the inverted pulsed electric field allows for the electro-elution of higher molecular weights.

11. Claims 8 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIKTOROWICZ et al. (U.S. Patent 6,214,191 B1) in view of NORDMAN et al. (U.S. PG-Pub 2002/0162745 A1), as applied to claims 1-7, 9, 10, 13, and 44-45, and in further view of ADCOCK (U.S. Patent 4,959,133).



a. With regards to claim 8, independent claim 5 and dependent claim 7 are obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. The combination of WIKTOROWICZ et al. and NORDMAN et al. discloses an integrated microfluidic device.

The combination of WIKTOROWICZ et al. and NORDMAN et al. does not appear to explicitly disclose an integrated microfluidic device wherein the DNA is greater than about 50 kilobases in size.

However, ADCOCK discloses a method of filed inversion electric pulses to force DNA or protein out of a gel and into an appropriate receiver (ABSTRACT). The inverted pulsed electric field allows for the electro-elution of higher molecular weights (line 57-60, column 2 such as "larger in molecular weight than  $2 \times 10^4$  base pairs").

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the integrated microfluidic device, as disclosed by the combination of WIKTOROWICZ et al. and NORDMAN et al., to include applying an inverted pulsed electric field, as disclosed by ADCOCK, because the inverted pulsed electric field allows for the electro-elution of higher molecular weights.

b. With regards to claim 14, independent claim 5 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. The combination of WIKTOROWICZ et al. and NORDMAN et al. discloses an integrated microfluidic device.

The combination of WIKTOROWICZ et al. and NORDMAN et al. does not appear to explicitly disclose an integrated microfluidic device wherein the two electrodes generate repeatedly inverted electric pulses.

However, ADCOCK discloses a method of filed inversion electric pulses to force DNA or protein out of a gel and into an appropriate receiver (ABSTRACT). The inverted pulsed electric field allows for the electro-elution of higher molecular weights (line 57-60, column 2 such as "larger in molecular weight than  $2 \times 10^4$  base pairs").

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the integrated microfluidic device, as disclosed by the combination of WIKTOROWICZ et al. and NORDMAN et al., to include applying an inverted pulsed electric field, as disclosed by ADCOCK, because the inverted pulsed electric field allows for the electro-elution of higher molecular weights.

12. Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIKTOROWICZ et al. (U.S. Patent 6,214,191 B1), as applied to claims 20-22, 24, and 46, and in further view of GAUTSCH (U.S. Patent 6,162,602).

a. With regards to claim 25 and 26, independent claim 20 is obvious over WIKTOROWICZ et al. under 35 U.S.C. 103(a) as discussed above. Modified WIKTOROWICZ et al. discloses an integrated microfluidic device comprising a section of matrix material.

Modified WIKTOROWICZ does not appear to explicitly disclose an integrated microfluidic device wherein the section of matrix material is an agarose gel plug.

However, GAUTSCH discloses a method for nucleic acid base sequencing and discloses separating fragments by means of capillary electrophoresis employing agarose or polyacrylamide gel (line 10-17, column 3).

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to substitute the section of matrix material in the integrated microfluidic device, as disclosed by modified WIKTOROWICZ et al., with an agarose gel plug, as disclosed by GAUTSCH, because the agarose gel is an improved method over slab gel and agarose is a functional equivalent to the polyacrylamide (GAUTSCH: line 10-17, column 3) and one with ordinary skill would have a reasonable expectation of success since both WIKTOROWICZ et al. and GAUTSCH are concerned with separating fragments.

13. Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIKTOROWICZ et al. (U.S. Patent 6,214,191 B1) in view of NORDMAN et al. (U.S. PG-Pub 2002/0162745 A1), as applied to claims 1-7, 9, 10, 13, and 44-45, and in further view of GAUTSCH (U.S. Patent 6,162,602).

a. With regards to claim 11 and 12, independent claim 5 is obvious over WIKTOROWICZ et al. in view of NORDMAN et al. under 35 U.S.C. 103(a) as discussed above. The combination of WIKTOROWICZ et al. and NORDMAN et al. discloses an integrated microfluidic device.

The combination of WIKTOROWICZ et al. and NORDMAN et al. does not appear to explicitly disclose an integrated microfluidic device wherein the section of matrix material is an agarose gel plug.

However, GAUTSCH discloses a method for nucleic acid base sequencing and discloses separating fragments by means of capillary electrophoresis employing agarose or polyacrylamide gel (line 10-17, column 3).

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to substitute the section of matrix material in the integrated microfluidic device, as disclosed by the combination of WIKTOROWICZ et al. and NORDMAN et al., with an agarose gel plug, as disclosed by GAUTSCH, because the agarose gel is an improved method over slab gel and agarose is a functional equivalent to the polyacrylamide (GAUTSCH: line 10-17, column 3) and one with ordinary skill would have a reasonable expectation of success since both modified WIKTOROWICZ et al. and GAUTSCH are concerned with separating fragments.

14. Applicant's arguments with respect to claims 1-26 have been considered but are moot in view of the new ground(s) of rejection.

a. Applicant argues that chamber 160 of WIKTOROWICZ et al. does not define an opening in the microfluidic device wherein a first and second electrode is disposed, as stated in the previous Final Office Action sent October 28, 2008. A different interpretation of the device of WIKTOROWICZ et al. is elaborated above to disclose these features.

b. Applicant argues that WIKTOROWICZ et al. does not disclose a matrix material only in the loading/unloading chamber. Applicant points out that WIKTOROWICZ et al. prefers liquid separation media. However, although the examiner concedes with applicant

that WIKTOROWICZ et al. does not appear to anticipate this limitation, it would have been obvious to use solid matrix type separation media for the reasons stated above. It is also acknowledged that while WIKTOROWICZ et al. may prefer liquid samples, the device, as disclosed, does not appear to exclusively limit separation within liquid media and is usable with solid type media, of which WIKTOROWICZ et al. admits is common practice.

c. Applicant argues that both ADCOCK and GAUTSCH do not cure the deficiencies of WIKTOROWICZ et al., especially since ADCOCK and GAUTSCH are concerned with solid matrix type separation. However, these arguments are believed to be addressed above with regards to the obviousness of solid matrix type separation in the device of WIKTOROWICZ et al.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DUSTIN Q. DAM whose telephone number is (571)270-5120. The examiner can normally be reached on Monday through Thursday, 7:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571)272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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dd  
April 24, 2009

/Alex Noguera/

Primary Examiner, Art Unit 1795

April 24, 2009